

### **REMARKS**

The Office Action mailed October 16, 2002 has been given careful consideration by the Applicants. The Examiner's recognition of allowable subject matter is acknowledged and appreciated. Nonetheless, Applicants respectfully request reconsideration of the application in light of the present amendments and the following comments.

#### **I. Rejection of Claims 1-3, 6, 9, 12, 14, 15, 17 and 18 Under §102(b)**

The Examiner rejected claims 1-3, 6, 9, 12, 14, 15, 17, and 18 under 35 U.S.C. §102(b) as being anticipated by U.S. Patent No. 5,246,866 to Nasu et al. The Examiner stated that Nasu teaches a DNA sequencing apparatus in which fluorescently labeled fragments are subject to electrophoresis and illuminated and exposed to detection to create an image corresponding to the gel. The Examiner further stated that while the Nasu scanner does require scanner to scan throughout the gel, the apparatus does achieve a full image within a given time duration.

Applicants respectfully submit that the rejected claims are not anticipated by Nasu. In particular, claims 1, 9, and 14, from which the remainder of the rejected claims depend, now specifically recites that the full image of the separation apparatus is generated in a single scan pass. Support for this amendment is found throughout the present specification, but particularly on Page 11, line 3 which states that "[i]t should be appreciated that in one embodiment a single pass of a scanner is used to collect the data." Thus, the present invention provides a technique for sequencing an entire sequencing plate (or separation apparatus) holding DNA fragments using known methods of DNA sequencing in combination with a full width scanner so that the image represents an entire sequencing plate during a single scan.

Nasu does not include each and every claimed element in the present invention. Specifically, the presently claimed subject matter (in independent claims 1, 9 and 14) calls for generating a *full image* of the separation apparatus and the separated DNA fragments *in a single scan pass*. Nasu, on the other hand, describes constantly scanning in the direction of migration using multiple scans. As such

Applicants respectfully request that the Examiner remove all rejections to claims 1-3, 6, 9, 12, 14, 15, 17 and 18 under §102(b), and allow the claims as amended.

## **II. Rejection of Claims 5 and 11 Under §103(a)**

The Examiner rejected claims 5 and 11 under §103(a) as being unpatentable over Nasu et al. in view of U.S. Patent No. 5,637,458 to Frankel et al. The Applicants respectfully disagree.

It is the Examiner's opinion that Nasu teaches all of the limitations of claims 5 and 11 except for the use of lithographically etched channels. It is the Examiner's opinion that Frankel teaches lithographically etched channels in glass substrates. Even assuming the propriety of combining the two references, such combination would still not render the present claims obvious. In this respect, newly amended independent claims 1 and 9, from which the rejected claims depend, calls for the generation of a full image of the separation apparatus in a single scan pass. As indicated, Nasu does not teach this feature. Frankel does not teach the generation of a full image of a separation apparatus in a single scan either. Therefore, the combination of the two references fails to disclose or suggest such a feature. As such, Applicants respectfully request that the Examiner remove the rejection of claims 5 and 11 under 35 U.S.C. §103(a) and allow the claims as amended.

## **III. Rejection of Claims 1-4, 6, 8-10, 12, 14, 15, and 18 Under §103(a)**

The Examiner also rejected claims 1-4, 6, 8-10, 12, 14, 15, and 18 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,274,240 to Mathies et al. in view of U.S. Patent No. 5,627,643 to Birnbaum et al. The Applicants respectfully disagree.

Applicants respectfully submit that the teachings of Mathies in view of Birnbaum do not render the presently claimed subject matter obvious. For example, claims 1 and 14 of the present application specifically call for sequencing DNA using a separation apparatus having a plurality of migration channels and generating a full image of the apparatus and the fragments in a single scan pass. Mathies states that "Birnbaum et al further teach the advantages of sequencing of the progress of separation process. It would have been

*prime facie* obvious to apply Birnbaum's full imaging to the plurality of channels in Mathies et al.'s device in order to increase throughput scanning." The Applicants respectfully submit that there is no motivation to combine the two references, and in fact, they cannot be combined.

At the time of Birnbaum's application (1993), the use of multiple channels in capillary electrophoresis of DNA molecules was known. The failure of Birnbaum to specifically indicate or teach the application of its whole capillary detection system to multiple capillary arrangement indicates the unobviousness of such a combination.

In addition, just because two references *can* be combined does not mean that it is obvious to do so. Here, there is no indication in Birnbaum or Mathies for the use of an arrangement disclosed in the other reference. To sustain an obviousness type rejection there must be some motivation to combine the references. Because there is no motivation to combine the references, the noted claims are not obvious under §103(a).

In addition, the Examiner rejected claim 19 under 35 U.S.C. §103(a) as being unpatentable over Mathies in view of Birnbaum in further view of U.S. Patent No. 6,136,612 to Della Ciana et al. However, claim 14 has already been established as distinguishable over the cited combination of Mathies and Birnbaum. Because claim 19 depends from claim 14 and because Della Ciana does not change the arguments relative to claim 14, claim 19 is also distinguishable. As such Applicants respectfully submit that claim 19 is not rendered obvious over Mathies in view of Birnbaum in further view of Della Ciana. Therefore, Applicants respectfully request that the Examiner remove the rejection of claim 19 and allow the claim.

#### **IV. Claims 7, 13, 16 and 20 are Patentable Over the References of Record.**

The Examiner indicated that claims 7, 13, 16 and 20 contained patentable subject matter. These claims have now been rewritten in independent form. The applicants respectfully submit that these claims are now allowable.

Claims 21-26 have been added. These claims depend from allowable claims 7 or 13, present no new matter and are submitted to be likewise allowable.

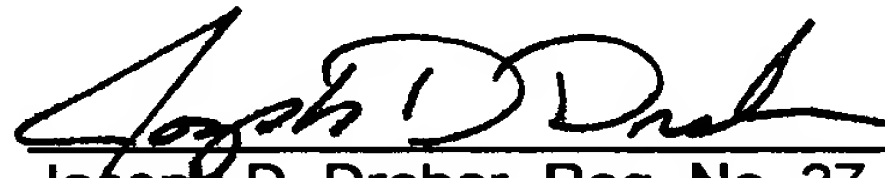
**CONCLUSION**

Applicants respectfully submit that the rejections and objections set forth by the Examiner in the Office Action mailed October 16, 2002 have been overcome. Accordingly, Applicants respectfully submit that claims 1-20 are now in condition for allowance. Withdrawal of the rejections and objections and early notification of allowability is earnestly solicited. Should any issues remain, the Examiner is encouraged to contact the undersigned to resolve any such issues.

Respectfully submitted,

FAY, SHARPE, FAGAN,  
MINNICH & MCKEE, LLP

Date: February 18, 2003

  
\_\_\_\_\_  
Joseph D. Dreher, Reg. No. 37,123  
Joseph E. Waters, Reg. No. 50,427  
1100 Superior Avenue  
Seventh Floor  
Cleveland, Ohio 44114  
216.861.5582

Attachment: Version with Markings to Show Changes Made

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

**In the Claims:**

1. (Twice Amended) A method of sequencing DNA fragments comprising:  
placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;  
applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;  
separating the DNA sample into fragments along the migration channel within the buffer;  
detecting fluorescent light emitted from the fragments along the migration channel; and,  
generating a full image of the separation apparatus and the separated DNA fragments [at a given time based on the detecting] in a single scan pass.

7. (Amended) [The method of claim 1 wherein the detecting comprises detecting using an amorphous silicon two-dimensional image sensor array] .A method of sequencing DNA fragments comprising:

placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

separating the DNA sample into fragments along the migration channel within the buffer;

detecting fluorescent light emitted from the fragments along the migration channel using an amorphous silicon two-dimensional image sensor array and,

generating a full image of the separation apparatus and the separated DNA fragments.

9. (Twice Amended) An apparatus for the sequencing of DNA comprising:

a separation apparatus having a plurality of migration channels operative to receive a DNA sample and facilitate migration and separation into fragments of the DNA sample along a migration channel within the apparatus;

a detector operative to detect light emitted from DNA fragments along the migration channels; and,

an image processor operative to generate image data representing a full image of the separation apparatus and the DNA fragments [at a given time] in a single scan pass.

13. (Amended) [The apparatus of claim 9 wherein the detector is a large area two-dimensional amorphous silicon image sensor array] An apparatus for the sequencing of DNA comprising:

a separation apparatus having a plurality of migration channels operative to receive a DNA sample and facilitate migration and separation into fragments of the DNA sample along a migration channel within the apparatus;

a two-dimensional amorphous silicon image sensor array detector operative to detect light emitted from DNA fragments along the migration channels; and,

an image processor operative to generate image data representing a full image of the separation apparatus and the DNA fragments.

14. (Twice Amended) A system for sequencing DNA fragments comprising:

means for placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

means for applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

means for separating the DNA sample into fragments along the migration channel within the buffer;

means for illuminating the DNA fragments;  
means for detecting fluorescent light emitted from the illumination fragments along the migration channel; and,  
means for generating a full image of the separation apparatus and the separated DNA fragments [at a given time based on the detecting] in a single scan pass.

16. (Amended) [The system of claim 14 wherein the detecting means comprises an amorphous silicon two-dimensional image sensor array] A system for sequencing DNA fragments comprising:

means for placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

means for applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

means for separating the DNA sample into fragments along the migration channel within the buffer;

means for illuminating the DNA fragments;

an amorphous silicon two-dimensional image sensor array for detecting fluorescent light emitted from the illumination fragments along the migration channel;  
and,

means for generating a full image of the separation apparatus and the separated DNA fragments.

20. (Amended) [The system of claim 14 wherein the illumination means comprises a laser attached to the rear of the detector] A system for sequencing DNA fragments comprising:

means for placing a DNA sample within a buffer in a separation apparatus having a plurality of migration channels;

means for applying an electric field across the separation apparatus to create a bias in the buffer such that the DNA sample migrates from one end of the apparatus to another end along a migration channel;

means for separating the DNA sample into fragments along the migration channel within the buffer;

a laser attached to the rear of the detecting means for illuminating the DNA fragments;

means for detecting fluorescent light emitted from the illumination fragments along the migration channel; and,

means for generating a full image of the separation apparatus and the separated DNA fragments.

Claims 21-26 have been added.

N:\XERZ\200339\US\la2196A.doc